SEQUENCE LISTING



Goldfarb, Valentina

<120> Modified Forms of Hepatitis C NS3 Protease for Facilitating Inhibitor Screening and Structural Studies of Protease:Inhibitor Complexes

<130> DB17Sequences

<140> 09/478,479

<141> 2000-01-06

<150> 60/115,271

<151> 1999-01-08

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<170> PatentIn Ver. 2.0 PatentIn Ver. 3.2

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<212> PRT

<213> Hepatitis C virus

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Glu Val Gln Ile Val Ser Thr Ala Ala Gln Thr Phe Leu Ala Thr Cys 35 40 45

Ile Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr 50 55 60

Ile Ala Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp
65 70 75 80

Lys Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr
85 90 95

Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala 100 105 110

Asp Val Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu 115 120 125

Ser Pro Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu

Leu Cys Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys 145 150 160 Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu 165 170 Glu Thr Thr Met Arg Ser 180 <210> 2 <211> 549 <212> DNA <213> Hepatitis C virus <400> 2 atggeteega teacegetta egeteageag accegtggte tgetgggttg cateateace 60 tccctgaccg gtcgtgacaa aaaccaggtt gaaggtgaag ttcagatcgt ttccaccgct 120 gctcagacct tcctggctac ctgcatcaac ggtgtttgct ggaccgttta ccacggtgct 180 ggtacccgta ccatcgcttc cccgaaaggt ccggttatcc agatgtacac caacgttgac 240 aaagacctgg ttggttggcc ggctccgcag ggttcccgtt ccctgacccc gtgcacctgc 300ggttcctccg acctgtacct ggttacccgt cacgctgacg ttatcccggt tcgtcgtcgt 360 ggtgactccc gtggttccct gctgtccccg cgtccgatct cctacctgaa aggttcctcc 420 ggtggtccgc tgctgtgccc ggctggtcac gctgttggta tcttccgtgc tgctgtttgc 480 accoggiggt tigctaaagc tgttgactic atcocggitg aatcoctgga aaccaccatg 540 cgttcctga 549 <210> 3 <211> 195 <212> PRT <213> Hepatitis C virus <400> 3 Met Lys Lys Gly Ser Val Val Ile Val Gly Arg Ile Val Leu Asn Gly Ala Tyr Ala Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr 25 Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Ile 35 Val Ser Thr Ala Ala Gln Thr Phe Leu Ala Thr Cys Ile Asn Gly Val 50 55 Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala Ser Pro 70 75 Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp Lys Asp Leu Val 85 Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys Thr Cys 105 Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro

115 120 125

Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro 135 140 130 Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Cys Pro Ala 150 155 Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val 170 Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu Glu Thr Thr Met 185 190 Arg Ser Pro 195 <210> 4 <211> 588 <212> DNA <213> Hepatitis C virus <400> 4 atgaaaaaa aaggttccgt tgttatcgtc ggccgtatag tactgaacgg tgcttacgct 60 cagcagactc gaggtctgct gggttgcatc atcacctccc tgaccggtcg tgacaaaaac 120 caggttgaag gtgaagttca gatcgtttcc accgctgctc agaccttcct ggctacctgc 180 atcaacggtg tttgctggac cgtttaccac ggtgctggta cccgtaccat cgcttccccg 240 aaaggtccgg ttatccagat gtacaccaac gttgacaaag acctggttgg ttggccggct 300 ccgcagggtt cccgttcct gaccccgtgc acctgcggtt cctccgacct gtacctggtt 360 acceptcacy etgacyttat eccepttegt cytegtggtg actecegtgg tteectgetg 420 teccegegte egateteeta eetgaaaggt teeteeggtg gteegetget gtgeeegget 480 ggtcacgctg ttggtatctt ccgtgctgct gtttgcaccc gtggtgttgc taaagctgtt 540 gacttcatcc cggttgaatc cctggaaacc accatgcgtt ccccgtga <210> 5 <211> 15 <212> PRT <213> Hepatitis C virus <400> 5 Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr <210> 6 <211> 15 <212> PRT <213> Hepatitis C virus <400> 6 Gln Gln Thr Arg Gly Glu Glu Gly Cys Gln Glu Thr Ser Gln Thr <210> 7

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20 25 30

Glu Thr Ser Gln Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val 35 40 45

Gln Ile Val Ser Thr Ala Ala Gln Thr Phe Leu Ala Thr Cys Ile Asn 50 55 60

Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala 65 70 75 80

Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp Lys Asp 85 90 95

Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys
100 105 110

Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val 115 120 125

Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro 130 135 140

Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys 145 150 155 160

Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys Thr Arg 165 170 175

Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu Glu Thr 180 185 190

Thr Met Arg Ser Pro 195

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ccggctggtc acgctgttgg tatcttccgt gctgctgttt gcacccgtgg tgttgctaaa 540 gctgttgact tcatcccggt tgaatccctg gaaaccacca tgcgttcccc gtga <210> 16 <211> 197 <212> PRT <213> Hepatitis C virus <400> 16 Met Lys Lys Gly Ser Val Val Ile Val Gly Arg Ile Asn Leu Ser Gly Asp Thr Ala Tyr Ala Gln Gln Thr Arg Gly Glu Glu Gly Cys Gln Glu Thr Ser Gln Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val 40 Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Cys Ile Asn 55 Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala Ser Pro Lys Gly Pro Val Thr Gln Met Tyr Thr Asn Val Asp Lys Asp Leu Val Gly Trp Gln Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys 105 . Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val 120 Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro 135 130 Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys 150 155 Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu Glu Thr 180 185 Thr Met Arg Ser Pro 195

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aaaaaccagg ttgaaggtga agttcagatc gtttccaccg ctacccagac cttcctggct 180 acctgcatca acggtgtttg ctggaccgtt taccacggtg ctggtacccg taccatcgct 240 tccccgaaag gtccggttac ccagatgtac accaacgttg acaaagacct ggttggttgg 300 caggeteege agggtteeeg tteeetgace eegtgeacet geggtteete egacetgtac 360 ctggttaccc gtcacgctga cgttatcccg gttcgtcgtc gtggtgactc ccgtggttcc 420 ctgctgtccc cgcgtccgat ctcctacctg aaaggttcct ccggtggtcc gctgctgtgc 480 ccggctggtc acgctgttgg tatcttccgt gctgctgttt gcacccgtgg tgttgctaaa 540 gctgttgact tcatcccggt tgaatccctg gaaaccacca tgcgttcccc gtga <210> 18 <211> 197 <212> PRT <213> Hepatitis C virus <400> 18 Met Lys Lys Gly Ser Val Val Ile Val Gly Arg Ile Asn Leu Ser 10 Gly Asp Thr Ala Tyr Ala Gln Gln Thr Arg Gly Glu Glu Gly Cys Gln Glu Thr Ser Gln Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val 40 Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Ser Ile Asn Gly Val Leu Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala Ser Pro Lys Gly Pro Val Thr Gln Met Tyr Thr Asn Val Asp Lys Asp 90 Leu Val Gly Trp Gln Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys 100 105 110 -Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val 120 Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro 130 135 140 Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys 145 150 Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Ser Thr Arg 170

Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu Glu Thr

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Thr Met Arg Ser Pro 195

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Lys Thr Ser His Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val

Gln Ile Val Ser Thr Ala Thr Gln Thr Phe Leu Ala Thr Ser Ile Asn 55

Gly Val Leu Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala 70

Ser Pro Lys Gly Pro Val Thr Gln Met Tyr Thr Asn Val Asp Lys Asp

Leu Val Gly Trp Gln Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys 100 105 110

Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val 115 120 125

Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro 135

Arg Pro Ile Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys 145

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Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Ser Thr Arg 165 170 Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Leu Glu Thr 180 185 Thr Met Arg Ser Pro 195 <210> 23 <211> 594 <212> DNA <213> Hepatitis C virus <400> 23 atgaaaaaa aaggatccgt tgttatcgtc ggccgtatca acctgtccgg tgacaccgct 60 tacgeteage agactegagg tgageagggt acceagaaga ceteceacae eggtegtgae 120 aaaaaccagg ttgaaggtga agttcagatc gtttccaccg ctacccagac cttcctggct 180 acctccatca acggtgttct gtggaccgtt taccacggtg ctggtacccg taccatcgct 240 tccccgaaag gtccggttac ccagatgtac accaacgttg acaaagacct ggttggttgg 300 caggeteege agggtteeeg tteeetgace cegtgeacet geggtteete egacetgtae 360 ctggttaccc gtcacgctga cgttatcccg gttcgtcgtc gtggtgactc ccgtggttcc 420 ctgctgtccc cgcgtccgat ctcctacctg aaaggttcct ccggtggtcc gctgctgtgc 480 ccggctggtc acgctgttgg tatcttccgt gctgctgttt ccacccgtgg tgttgctaaa 540 gctgttgact tcatcccggt tgaatccctg gaaaccacca tgcgttcccc gtga <210> 24 <211> 197 <212> PRT <213> Hepatitis C virus <400> 24 Met Lys Lys Lys Gly Ser Val Val Ile Val Gly Arg Ile Asn Leu Ser Gly Asp Thr Ala Tyr Ala Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly Glu Val 35 40 Gln Ile Val Ser Thr Ala Ala Gln Thr Phe Leu Ala Thr Cys Ile Asn 50 Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Thr Arg Thr Ile Ala 70 75 Ser Pro Lys Gly Pro Val Ile Gln Met Tyr Thr Asn Val Asp Lys Asp Leu Val Gly Trp Pro Ala Pro Gln Gly Ser Arg Ser Leu Thr Pro Cys · 105 100

125

Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val

120

115

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                                            140
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Pro Ala Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys Thr Arg
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51

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      (22)..(22)
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      (30)..(30)
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                                   10
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      (19)..(19)
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<221> misc_feature
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      (34)..(34)
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ggccgtatca wcctgtccra cggtaccgct tackctcagc agac
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      (30)..(30)
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<223> wherein m = a or c
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                                                                     44
<210> 39
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<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> wherein Xaa = Asn or Ile
<220>
<221> MISC_FEATURE
<222> (14)..(14)
```

```
<223> wherein Xaa = Ser or Ala
<400> 39
Gly Arg Ile Xaa Leu Ser Asp Gly Gly Ile Thr Ala Tyr Xaa Gln Gln
Thr
<210> 40
<211> 50
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222>
      (11)..(11)
<223> wherein w = a or t
<220>
<221> misc_feature
<222>
      (40)..(40)
<223> wherein k = g or t
<400> 40
                                                                      50
ggccgtatca wcctgtccga cggtggtatc accgcttack ctcagcagac
<210> 41
<211> 50
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222>
      (7)..(7)
<223>
      wherein w = a or t
<220>
<221>
      misc_feature
      (36) . . (36)
<222>
<223> wherein m = a or c
<400> 41
                                                                      50
catagtwgga caggctgcca ccatagtggc gaatgmgagt cgtctgagct
<210> 42
<211> 15
<212> PRT
<213> Hepatitis C Virus
```

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<400> 42

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Gly Arg Ile Asn Leu Ser Gly Asp Thr Ala Tyr Ala Gln Gln Thr
               5 .
                                   10
<210> 43
      39
<211>
<212> DNA
<213> Hepatitis C Virus
<400> 43
acgggaaccc tgcggagctg ccaaccaacc aggtctttg
                                                                     39
<210> 44
<211> 55
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
      (37)..(37)
<222>
<223> wherein r = a or g
<400> 44
caacgttggt gtacatctgg gtaaccggac ctttcgrgga agcgatggta cgggt
                                                                     55
<210> 45
<211>
      37
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222>
      (19)..(19)
<223> wherein m = a or c
<400> 45
                                                                     37
ccaggaaggt ctgggtagmg gtggaaacga tctgaac
<210> 46
<211> 40
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222> (22)..(22)
<223> wherein w = a or t
<400> 46
```

```
40
ctttagcaac accacgggtg gwaacagcag cacggaagat
<210> 47
<211>
      52
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222>
      (21)..(21)
<223> wherein k = g or t
<220>
<221> misc_feature
      (36)..(36)
<222>
<223> wherein w = a or t
<400> 47
                                                                    52
accgtggtaa acggtccaca kaacaccgtt gatggwggta gccaggaagg to
<210> 48
<211>
      78
<212> DNA
<213> Hepatitis C Virus
<220>
<221> misc_feature
<222> (21)..(21)
<223> wherein k = g or t
<220>
<221> misc_feature
<222>
      (36)..(36)
<223> wherein w = a or t
<220>
<221> misc_feature
<222> (60)..(60)
<223> wherein m = a or c
<400> 48
                                                                     60
accgtggtaa acggtccaca kaacaccgtt gatggwggta gccaggaagg tctgggtagm
                                                                     78
ggtggaaacg atctgaac
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